REMARKS

I. Status of the claims

Claims 1, 4, 6, and 13 are pending. Claim 3 has been canceled. Claim 1 has been amended to further specify that the reaction medium is a polar organic solvent, which was set forth in the canceled dependent claim 3. Claim 4 has been amended to address the correct dependency, and the amended claim 4 has the same limitation as previously presented.

No new matter has been introduced through these amendments. Because the claims have only been amended to include the recitation set forth the in the dependent claim, the amendment does not necessitate a new search. Additionally, the amendments present the rejected claims in condition for allowance or in better condition for appeal. As such, entry of these amendments is respectfully requested.

II. Rejections under 35 U.S.C. § 103(a)

The examiner has rejected claims 1, 3, 4, 6, and 13 under 35 U.S.C. § 103(a) as being unpatentable over the article by Tobe et. al. entitled "Discovery of Quinazolines as a Novel Structural Class of Potent Inhibitors of NF-κB Activation" Bioorg. Med. Chem., 2003, vol. 11, no. 3, p. 383-391 ("Tobe"), in view of the book by Turner entitled "The Design of Organic Syntheses" Elsevier, 1976, p. 10 and p. 149 ("Turner"), the article by Mayer et al. entitled "Enzyme-initiated domino (cascade) reactions" Chem Soc. Rev., 2001, 30, p. 332 ("Mayer"), the article by Chen et al. entitled "Parallel Differentiated Recognition of Ketones and Acetals" Angewandte Chemie Int. Ed., 1998, 37, no. 1/2, p. 91-93 ("Chen"), and the citation from Science, 21 October 2005, vol. 310, p. 409 ("Science"), U.S. Patent No. 4,138,433 to Kleiner et al. ("Kleiner") and U.S. Patent No. 4,081,455 to Kuhla ("Kuhla").

The examiner states that Tobe teaches that the 2-aminophenyl carboxylic acid compound (formula 7) is processed with aqueous ammonia solution (formula 2), followed by reaction with trimethylformate (formula 4) in sequential steps at room temperature and cooling, respectively. See Office Action, p. 3. According to the examiner, Tobe is different from Applicants' invention in a) aqueous ammonia solution used in Tobe versus Applicants' polar organic solvent and b) the sequential step reaction in Tobe versus Applicants' one-pot reaction. The examiner tries to cure Tobe's deficiency by citing Turner, Mayer, Chen, Science, Kleiner and Kuhla, which allegedly teach that integration of multistep chemical reactions into one-pot process without isolating and purifying the intermediates are advantageous. The examiner subsequently conclude that

variation from Tobe's sequential step reaction to Applicants' one-pot reaction would have been obvious to one skilled in the art. See Office Action, p. 4-5. In addition, the examiner asserts that because ammonia can be commercially purchased in ethanol and the reaction may proceed with either solvent present in the reaction, these two solvents are alternatively usable. See Office Action , p. 4. Applicants respectfully traverse this rejection at least for reasons advanced in detail below.

The examiner states that "the sole difference between the claimed process and Tobe's process is Tobe purifies the intermediate and then proceeds to the next step, whereas Applicants do the step consecutively without isolation of the intermediate." See Office Action, p. 4. Applicants respectfully disagree with the examiner's statement. The difference between the claimed process and Tobe's process is more than simply adding Tobe's reagents consecutively in one-pot to eliminate the step of isolating and purifying the intermediates.

Tobe contains two separate reaction steps. In Tobe, a 2-aminophenyl carboxylic acid compound (formula 7) is reacted with EDC (N-ethyl-N'-[3-(dimethylamino)propyl] carbodiimide) and HOBt (1-hydroxybenzotriazole) in 28% aqueous ammonia solution to give an aminobenzamide compound (formula 8), which is subsequently reacted with trimethylformate in 12N HCl to give a quinazoline compound (formula 9). See description synthetic pathway of Scheme 2 on p. 384, and the third and fourth paragraphs in the left-hand column on p. 388. In contrast, the method of the claimed invention recites only one reaction step. What is remarkable about the claimed process is Applicants' discovery that the target pyrimidin-4-one compound of formula (7) can be obtained in one reaction step by reacting an aminocarboxylic acid compound of formula (6) with a combination of the organic acid compound of formula (4) and a nitrogen atom-containing compound of formula (2) in a polar organic solvent. No amidation reagent such as the combination of EDC (N-ethyl-N'-[3-(dimethylamino)propyl]carbodiimide) and HOBt (1-hydroxybenzotriazole) is used in Applicants' claimed reaction. Hence, the claimed process would proceed without the production of the amide compound of formula 8 produced in Tobe's reaction. In another word, Applicants' claimed reaction process does not contain the intermediate of Tobe's sequential steps, and hence is distinctive over Tobe's sequential steps. Tobe does not teach or suggest the claimed one-step process with the claimed reagents. Nor does any of Turner, Mayer, Chen, Science, Kleiner and Kuhla teach or suggest that the claimed reagents can be used to produce the target pyrimidin-4-one compound of formula (7) in the claimed one-step reaction.

Moreover, Tobe's two-step reactions can not be conducted in one pot. As described above, the first step of Tobe's reaction is performed in an aqueous ammonia solution (i.e., aqueous basic solution), and the second step of Tobe's reaction is performed in an aqueous 12N HCl solution (i.e., aqueous acidic solution). Apparently, Tobe's first step and second step should be processed in different reaction media having opposite nature from each other, i.e. the first step of Tobe requires acid solution and the second step of Tobe requires a basic solution. If Tobe's two-step reactions are consecutively run in the same vessel (i.e., one-pot) without isolation of the intermediate produced in the first step, the second step reaction would have been run in the mixture of the aqueous ammonia solution and the aqueous HCl solution. If so, the second step reaction would have not been successful in the one-pot process because the reaction condition of the second step in the one-pot process would have been different from that disclosed in Tobe. Consequently, the two sequential step reactions in Tobe can not be performed in one-pot due to the mutually exclusive natures of the reaction media required for the two different reaction steps.

The examiner cites Turner to show that when carrying out multistep reactions, one-pot process is preferred to sequential step reactions because the step of isolating the reaction intermediate is eliminated. However, the prerequisite of integrating multi-step reactions into one-pot process is that the reaction media for multi- sequential steps should be the same so that the reagents from different reaction steps can be consecutively added and the one-pot process can be performed in the same reaction medium. This prerequisite has also been disclosed in Turner cited by the examiner: "If several steps are necessary, 'A' to 'B' to 'C', ideally they should be carried out consecutively in the same medium, without isolation of the intermediates." See Office Action, page 4. Thus, the prior art references cited by the examiner clearly teach away from varying Tobe's two-step reactions to a one-pot process, alleged by the examiner.

Regarding the solvent used in Tobe's reaction, Tobe only teaches the use of 28% aqueous ammonia solution in the first reaction step of obtaining an aminobenzamide compound from an aminocarboxylic acid compound. Tobe is completely silent relating to the use of the ammonia in ethanol as a reaction medium in a one-pot, one-step reaction to obtain a pyrimidin-4-one compound of formula (7) from an aminocarboxylic acid compound of formula (6). Neither does any of the other cited prior art references suggest or disclose that ammonia in ethanol can be used as a reaction medium in the claimed one-pot, one-step reaction. The examiner states that the reaction may proceed with either solvent present in the reaction and these two solvents are alternatively usable. However, the examiner has not provided any grounds for such a

statement. MPEP § 2143.01 states that the mere statement that the claimed invention is within the capabilities of one of ordinary skill in the art is not sufficient by itself to establish prima facie obviousness. Therefore, the reaction medium used in the claimed one-pot, one-step reaction process, namely a polar organic solvent in the presence of a nitrogen atom-containing compound of formula (2) is used to obtain a pyrimidin-4-one compound of formula (7) from an aminocarboxylic acid compound of formula (6), is not obvious over Tobe.

For the reasons discussed above, Tobe in view of Turner, Mayer, Chen, Science, Kleiner and Kuhla does not render Applicants' invention obvious. Accordingly, Applicants therefore respectfully request that the examiner withdraw this rejection of claims 1, 3, 4, 6, and 13 under 35 U.S.C. § 103(a).

III. Conclusion

Applicants request reconsideration of this application in view of the remarks set forth above, and allowance of this application.

Except for issue fees payable under 37 C.F.R. §1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account No. 19-2380. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. §1.136(a)(3).

Respectfully submitted,
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